

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

DR. FALK PHARMA GMBH,
Petitioner,

v.

ELLODI PHARMACEUTICALS, L. P.,
Patent Owner.

Case No. IPR2024-01197
Patent No. 8,771,729 B2

PATENT OWNER'S RESPONSE

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List of Patent Owner's Exhibits

Exhibit No.	Description
2007	Declaration of Martyn Christopher Davies in Support of Patent Owner's Response
2008	<i>Curriculum Vitae</i> of Martyn Christopher Davies
2009	U.S. Patent Application Publication No. 2005/0009848 A1 ("Brantl")
2010	Clinical Trials Study, "Efficacy, Safety, and Pharmacokinetics of APT-1011 in Subjects With Eosinophilic Esophagitis (EoE)(FLUTE)," last updated Apr. 26, 2023, https://clinicaltrials.gov/study/NCT03191864?tab=results&a=11#outcome-measures
2011	Deposition of Alan F. Parr, Pharm.D., Ph.D., dated April 9, 2025
2012	"Antrum" Definition, American Medical Dictionary: A Concise and Up-to-Date Guide to Medical Terms (1998)
2013	M.E. Aulton (Ed.), <i>Pharmaceutics: The Science of Dosage Form Design</i> (2d. 2002)
2014	"Lozenge" Definition, Dennis B. Worthen (ed.), <i>Dictionary of Pharmacy</i> (2004)
2015	Paul J. Sheskey et al., <i>Handbook of Pharmaceutical Excipients</i> (8d. 2017)

I. INTRODUCTION

The challenged claims of U.S. Patent No. 8,771,729 (“the ’729 patent”) relate to an orally disintegrating solid pharmaceutical composition comprising a topically active corticosteroid¹ (i.e., a corticosteroid with no significant systemic glucocorticoid or mineralocorticoid activity) that disintegrates within 60 seconds or less according to the USP<701> test. The pharmaceutical composition topically deposits the corticosteroid in the upper gastrointestinal tract to treat an inflammatory condition of the upper gastrointestinal tract, such as eosinophilic esophagitis (EoE). Ex. 1001, 1:11-26, 5:11-15. Some claims further require the pharmaceutical composition to disintegrate within 30 seconds and that the topical corticosteroid is deposited on the esophagus. Petitioner’s proposed prior art, even when considered in combination, fails to provide motivation or a reasonable expectation to arrive at the claimed invention. Accordingly, Petitioner has not met its burden of proving the challenged claims of the ’729 patent would have been obvious.

The Board instituted review on all grounds outlined in the Petition. In Grounds 1 and 3, Petitioner asserts that claims 1-7, 15, 20-21, 27, 29-36 would have

¹ As used herein, “topical corticosteroid” refers to a corticosteroid having no significant systemic glucocorticoid or mineralocorticoid activity as defined in the ’729 patent.

been obvious over US 2007/0111978 (“Dohil”) and claims 8, 16-18 would have been obvious over Dohil and US 2005/0232988 (“Venkatesh”). But Dohil does not teach an orally disintegrating solid pharmaceutical composition that disintegrates within 60 seconds or less in the mouth, let alone provide motivation or a reasonable expectation of success in arriving at such a pharmaceutical composition to treat EoE. It teaches a “simple” and “palatable” viscous liquid composition that provides “pan-esophageal mucosal coverage” to effectively treat EoE, with only a passing reference to solid compositions. Ex. 2011, 72:25-74:6, 61:3-9, 66:17-20, 68:10-12, 68:22-24, 70:8-12; Ex. 1002, [0067]. Venkatesh is directed generally to formulating orally disintegrating tablets containing microgranules and taste-masked microcapsules to improve taste and mouthfeel by shielding bad-tasting drugs from contacting the mouth and consequently the esophagus by coating the bad-tasting drugs with certain polymers. Ex. 2011, 89:1-18; 90:13-92:18; 93:12-16; 94:4-25; Ex. 1020, [0027]. It does not teach or suggest an orally disintegrating solid pharmaceutical composition that topically deposits a topically acting drug in the upper gastrointestinal tract (e.g., esophagus) for treating an inflammatory condition thereof (e.g., EoE).

Petitioner uses a hindsight-driven analysis to presume that a person of ordinary skill in the art (POSA) would be seeking to formulate a solid pharmaceutical composition that disintegrates within 60 seconds or less in the mouth based on the disclosure in Dohil. Petitioner provides no basis for the motivation to

start from a solid, instead of Dohil's exemplified liquid formulation that was tested and shown to be effective. Neither the general knowledge of a POSA nor Venkatesh can remedy this deficiency. The petition and expert declaration failed to identify, or even search for, a prior art orally disintegrating tablet used to deliver a topical drug to the upper gastrointestinal tract, and Venkatesh's formulation is specifically designed to avoid topical contact with the mouth and upper gastrointestinal tract. Ex. 2011, 17:8-15.

In Grounds 2 and 4, Petitioner asserts that claims 1-7, 9-15, 20, 27-28, 35-36, 38-40 would have been obvious over WO 00/44351 ("Grother") and the FDA Guidance for Industry: Orally Disintegrating Tablets (2008) ("FDA Guidance") and claims 8, 16-26, 37 would be obvious over Grother, the FDA Guidance, and Venkatesh. Grother is not directed to any disease and does not teach orally disintegrating solid pharmaceutical compositions designed to topically deposit a topical (non-systemically active) drug in the upper gastrointestinal tract for the treatment of inflammation of the upper gastrointestinal tract. Instead, it teaches a general "fast dispersing solid dosage form[]" platform that does not use gelatin and can be used with any active drug. Ex. 1008, Abstract. Similarly, the FDA Guidance is not directed to any particular disease, drug, or topical delivery of drugs to the upper gastrointestinal tract. It simply provides a definition for orally disintegrating tablets ("ODTs") as disintegrating within 30 seconds as measured by the United

States Pharmacopeia (USP) <701> Disintegration Test. Ex. 1005, 2-3. It does not teach any ODT formulations or topical corticosteroids. Petitioner again relies purely on impermissible hindsight, and as with Grounds 1 and 3, Petitioner offers no real reason why a POSA would have been motivated to formulate a solid pharmaceutical composition containing a topical corticosteroid that disintegrates in 60 second to topically deposit the corticosteroid on the upper gastrointestinal tract to treat inflammatory conditions thereof.

Because the Petition is factually and legally deficient, the Board should confirm the patentability of all challenged claims.

II. BACKGROUND

A. The '729 Patent (Ex. 1001)

The '729 patent is directed to orally disintegrating solid pharmaceutical compositions containing a topically active corticosteroid that topically administers a therapeutically effective amount of a corticosteroid to inflamed tissue of the upper gastrointestinal tract for the treatment of conditions associated with inflammation of the upper portion of the gastrointestinal tract. Ex. 1001, 1:11-26, 5:11-15. One condition, eosinophilic esophagitis (EoE), is an inflammatory condition of the esophagus. Ex. 1001, 1:24-26. Prior treatments for EoE included corticosteroid formulations designed for inhalation that were instead applied to the back of the throat, (Ex. 1001, 1:30-41), as well as oral administration of systemically active

corticosteroids (Ex. 1001, 1:42-50). These treatments posed undesirable side effects, including candidiasis infection and suppression of immune function, respectively. Ex. 1001 at 1:30-50.

The orally disintegrating solid pharmaceutical composition claimed in the '729 patent solves these problems by formulating a solid pharmaceutical composition with a corticosteroid that has no significant systemic glucocorticoid or mineralocorticoid activity after oral administration (i.e., a topically active corticosteroid). The orally disintegrating solid dosage form disintegrates within 60 seconds and topically deposits the corticosteroid to the upper gastrointestinal tract, including the esophagus. Ex. 1001, 1:56-67. This mechanism of localized delivery mitigates the undesirable side effects of traditional EoE treatments. Ex. 1001, 1:56-67, 3:62-66. It is surprising that the claimed pharmaceutical composition mitigates candidiasis since an orally disintegrating composition would remain in the oral cavity longer than formulations designed for inhalation that are instead applied to the back of the throat. Ex. 1031, 32; *see also* Ex. 2010, 89. It is also surprising that the claimed pharmaceutical composition “topically provide[s] a therapeutically effective amount of a corticosteroid to inflamed tissues of the gastrointestinal tract, after oral administration” given the significant mechanistic and structural differences compared to Dohil’s viscous liquid formulation. Ex. 1001, 5:12-15.

B. Prosecution of the '729 Patent (Ex. 1031)

The '729 patent issued from U.S. Patent Application No. 12/896,005 (“the '005 Application”). Ex. 1001, cover. Patent Owner filed the '005 Application on October 1, 2010. Ex. 1001, cover. During prosecution, the Examiner rejected the as-filed claims for obviousness over US 2009/0169620 (“Venkatesh 2009”) in view of US 2005/0009848 (“Brantl”) and Venkatesh 2009 in view of Brantl, and in further view of US 2007/0059361 (“Rawas-Qalaji”). Ex. 1031, 85-96. The Examiner argued that Venkatesh 2009 teaches a solid pharmaceutical composition in the form of an orally disintegrating tablet (ODT) that disintegrates within 60 seconds or less and Brantl teaches the administration of topical corticosteroids. *Id.* Patent Owner responded to the Examiner’s rejection, asserting that Venkatesh 2009 does not teach the topical administration of corticosteroids and, in Brantl, corticosteroids are optional, and when used, the entire dosage form is enterically coated² to deliver the

² Notably, the vast majority of prior art budesonide formulations cited by Petitioner are enterically coated. As such, these compositions cannot topically administer budesonide to the upper gastrointestinal tract, because the enteric coating prevents budesonide from being topically deposited on the gastrointestinal tract until the enteric coating dissolves after it passes through the stomach, to the intestines. Ex. 2007, ¶¶ 64-72.

corticosteroid to intestines, after passing through stomach Ex. 2009, [0033], [0058]; Ex. 1031, 71-76; *see also* Ex. 2009, [0081]. To further distinguish over such enterically coated formulations, the claims were amended to recite that “upon administration the corticosteroid is deposited topically in the upper gastrointestinal tract.” Ex. 1031, 65.

The Examiner subsequently withdrew this rejection but made another obviousness rejection over US 2009/0131386 (“Phillips”) in view of Venkatesh 2009 and Rawas-Qalaji. Ex. 1031, 42-54. The Examiner argued that Phillips³ teaches solid pharmaceutical compositions for the treatment of inflammation of the gastrointestinal tract. *Id.* Patent Owner responded to the Office Action, arguing that Phillips is directed primarily to liquid dosage forms and does not teach an orally disintegrating solid pharmaceutical composition that can disintegrate within 60 seconds. Ex. 1031, 30-34. Patent Owner also amended claim 1 to specify that the pharmaceutical composition is an “orally disintegrating” solid pharmaceutical composition that contains “at least one disintegrant[.]” Ex. 1031, 25. The Examiner withdrew the rejection based on Phillips and allowed the claims, noting that Phillips did not disclose the disintegration time. Ex. 1031, 19.

³ Phillips is equivalent to Dohil. *See* Patent Owner’s Preliminary Response, 12-20.

III. THE LEVEL OF ORDINARY SKILL IN THE ART

In this proceeding only, Patent Owner generally accepts Petitioner's proposed level of ordinary skill in the art.

IV. CLAIM CONSTRUCTION

In this proceeding only, Patent Owner generally accepts Petitioner's proposed constructions.

V. PETITIONER FOCUSES ON IRRELEVANT BACKGROUND PRIOR ART

In describing the state of the prior art, Petitioner focuses on irrelevant and undisputed prior art disclosing budesonide and orally disintegrating pharmaceutical compositions, none of which is relied on in Petitioner's or its expert's obviousness analysis. Ex. 2011, 31:20-21, 41:1-15. Petitioner asserts, and Patent Owner does not dispute, that budesonide for the treatment of inflammatory conditions and orally disintegrating pharmaceutical compositions were known in the prior art.

Petitioner cites to various references, including Petitioner's product Budenofalk, as teaching the use of budesonide for treating inflammatory conditions such as Crohn's disease and ulcerative colitis. Pet., 5 (citing Exs. 1025, 1009, 1010, 1011, 1012, 1013, 1026, 1027, 1028). These references all relate to the use of budesonide for treating inflammation of the lower gastrointestinal tract, largely using enterically coated budesonide tablets designed to deliver budesonide to the lower gastrointestinal tract. Ex. 2007, ¶¶, 64-72. Petitioner does not rely on any of

these background references in its obviousness analysis, nor are any of these references relevant to the problems solved by the '729 patent. Ex. 2007, ¶¶ 64-76.

Petitioner goes on to cite Aceves et al. 2005 and 2007, which were included in Dohil's Examples. Pet., 5-6 (citing Ex. 1014, 1015). As Petitioner points out, Aceves 2005 and 2007 reported successful treatment of EoE with a viscous liquid suspension of budesonide. Pet., 5 (citing Ex. 1014, 706; Ex. 1015, 1, 6, 8). The viscous liquid suspension of budesonide and its successful treatment in EoE was then published in Dohil. Petitioner does not rely on any of these background references in its obviousness analysis, nor are any of these references relevant to the problems solved by the '729 patent. Ex. 2007, ¶¶ 73-76.

Orally disintegrating pharmaceutical compositions were also known in the art for easy administration of *systemically active drugs to the stomach and lower intestines*, and promoting absorption. Petitioner cites to several references that highlight these advantages of using orally disintegrating pharmaceutical compositions. Pet., 8 (citing Ex. 1019, 310-311; Ex. 1018, 466-67; Ex. 1017, 172). Petitioner further refers to a list of commercially available orally disintegrating pharmaceutical compositions. Pet., 8-9. None of the compositions contain topically acting corticosteroids or were used to treat an inflammatory condition of the upper gastrointestinal tract or EoE. Ex. 2007, ¶¶ 78-79. Indeed, neither the Petition nor Petitioner's expert provided any evidence of an orally disintegrating pharmaceutical

composition used for topical delivery of a topically active drug to the upper gastrointestinal tract, and the expert admits he was not aware of any such formulation in the prior art. Ex. 2011, 18:5-8.

A. Petitioner’s Analysis of the Prior Art is Guided by Impermissible Hindsight

Before reaching the grounds for obviousness, Petitioner analyzes the scope of the prior art through the lens of impermissible hindsight, because Petitioner is focused on the claimed orally disintegrating tablets, not finding EoE treatments. “The invention must be viewed not with the blueprint drawn by the inventor, but in the state of the art that existed at the time.” *Interconnect Planning Corp. v. Feil*, 774 F.2d 1132, 1138 (Fed. Cir. 1985). As explained further below, neither the Petition nor Petitioner’s expert explain why a POSA would have been motivated to make an orally disintegrating solid pharmaceutical composition containing a topical corticosteroid that disintegrates within 60 seconds, or a reasonable expectation in topically depositing the topical corticosteroid in the upper gastrointestinal tract in an effective amount to treat an inflammatory condition thereof.

Rather than explaining how or why the asserted references are combined to arrive at the claimed invention, Petitioner defines the scope of the prior art starting with orally disintegrating tablets using the blueprint provided by the ’729 patent, which is impermissible. Perhaps the most striking evidence of Petitioner’s

hindsight-driven analysis is its expert's admission that it was not aware of and conducted no specific search for any prior art orally disintegrating composition used to deliver a topically acting drug to the esophagus. Ex. 2011, 18:5-13 ("Q: Are you aware of any drugs that have been developed as an ODT for topical administration of the esophagus? A: No, I do not...Q: You didn't do any investigation into that for this declaration, correct? A: No, ma'am").

1. Dohil

Petitioner cites to Dohil for its disclosure of a "lozenge or similar tablet" that dissolves rapidly in the mouth or esophagus as teaching an orally disintegrating solid pharmaceutical composition. Pet., 10. However, Dohil is mainly directed to liquid compositions containing viscosity enhancing agents that improve contact of the corticosteroid with the esophagus. Petitioner only cites to three paragraphs in Dohil which generally refer to solid dosage forms. Pet., 6, 10; Ex. 2007, ¶¶ 81-82. The remaining disclosure in Dohil, which spans approximately 110 paragraphs, is exclusively related to liquid formulations of budesonide. All three examples in Dohil discuss an oral viscous liquid budesonide formulation (referred to as OVB) that effectively treats EoE in children and has several advantages, including palatability and effective drug contact with the esophagus. Ex. 1002, [0067] ("It may have advantages over other therapies in that it is palatable, its volume (8-12 ml) provides pan-esophageal mucosal coverage and it requires only once daily

administration.”); *id.*, [0056]-[0070]. Dohil does not mention any problems with the viscous liquid formulation and no solid form of budesonide is exemplified in Dohil. Ex. 2007, ¶ 81.

Dohil teaches that it “is often difficult to deliver an effective dose of corticosteroid to the targeted area of the esophagus.” Ex. 1002, [0007]. To solve this problem, Dohil teaches “[a] liquid, long-acting topical corticosteroid preparation is needed.” Ex. 1002, [0009]. Dohil’s liquid compositions are formulated with a viscosity enhancer to deliver to the esophagus a viscous liquid containing budesonide that coats the esophagus. Ex. 1002, [0011], [0013], [0021], [0038], [0042]-[0045], [0046], [0048]-[0070]. Dohil also teaches that a large volume of the budesonide formulation is necessary to provide an effective amount of the corticosteroid to the esophagus. Ex. 1002, [0031], [0053], [0067] (“[OVB] may have advantages over other therapies in that...its volume (8-12 ml) provides pan-esophageal mucosal coverage...”). Taken together, a POSA would understand Dohil as teaching that a specific, large volume (8-12 mL) of a viscous liquid formulation solves the problems Dohil identified by coating the esophagus and topically delivering an effective dose of a topical corticosteroid to the esophagus to treat EoE. Thus, Petitioner’s interpretation of Dohil as providing motivation to formulate the claimed orally disintegrating composition is pure hindsight. Ex. 2007, ¶ 81.

While Dohil mentions a “lozenge or similar tablet” that dissolves rapidly, this does not lead a POSA to the claimed invention. When read as a whole, a POSA would understand that Dohil’s lozenge or similar tablet would provide an initial rapid release of drug and then dissolve slowly to provide the large volume of viscous liquid that Dohil teaches is required to coat the esophagus and treat EoE. Ex. 2007, ¶ 82. A POSA would understand this because a lozenge – based on the art-recognized definition – does not contain a disintegrant and is sucked on by patients and continuously dissolves slowly over time, as described in Petitioner’s own cited references. Ex. 2007, ¶ 82; Ex. 1017, 181; *see also* Ex. 2013, 413; Ex. 2014, 201. Indeed, Petitioner’s expert also admits that a typical lozenge dissolves slowly. Ex. 2011, 62:13-15. None of Petitioner’s art refers to any quick or rapidly dissolving lozenges, nor was its expert able to identify any fast dissolving lozenge. Ex. 2011, 63:6-21. A tablet similar to a lozenge would, therefore, need to function the same in terms of its dissolution rate.

Petitioner points to the fact that Dohil describes its lozenge or similar tablet as dissolving rapidly, as teaching the claimed invention. Pet., 10. Dohil, however, does not define “lozenge” or “dissolve rapidly.” In fact, Dohil goes on to state that “for children or other patients that may have difficulty with a dissolving lozenge, the lozenge may be ground or otherwise dissolved in a small volume of water or other pharmaceutically suitable liquid[.]” Ex. 1002, [0032]. Petitioner explains that solid

dosage forms that disintegrate within 60 seconds are easy to swallow which is desirable for pediatric patients. Pet., 7-8. Following that logic, if Dohil's lozenge dissolved that quickly, children would likely not have difficulties with it. Thus, a POSA would understand the "lozenge or similar tablet" to be a distinctly different type of oral dosage form than claimed. Ex. 2007, ¶ 85.

The same paragraph in Dohil includes reference to a "slow release" tablet, capsule, or gel capsule. Ex. 1002, [0032]. "Slow release" is also not defined. As noted above, a POSA reading Dohil would understand that based on the definition of a lozenge in the art, "dissolve rapidly" would refer to the initial release of some drug, but that complete dissolution would occur over time. Ex. 2007, ¶ 83. Based on the disclosure of "slow release" tablets in the same paragraph, a POSA would understand that Dohil discloses solid dosage forms that release budesonide over an extended period of time in the mouth as a lozenge or slow release tablet. Ex. 2007, ¶ 84.

Interpreting Dohil to teach disintegration within 60 seconds reads into Dohil a disclosure that simply isn't there, which is evidence of hindsight. Petitioner starts with the claim language of the '729 patent and attempts to force Dohil's disclosure to fit into the claims of an orally disintegrating solid pharmaceutical composition comprising a corticosteroid that disintegrates within 60 seconds. As explained in further detail below, Petitioner fails to provide the requisite motivation to combine

Dohil with the knowledge of a POSA and Venkatesh to arrive at the claimed invention.

2. Grother

Petitioner also cites to Grother as disclosing a solid orally disintegrating composition of budesonide. Pet., 10 (citing Ex. 1008). The Petitioner's reliance on Grother is based purely on impermissible hindsight because, as confirmed by Petitioner's expert, Grother is not directed to any particular disease and does not teach topical deposition of a topically active drug to the upper gastrointestinal tract (e.g., esophagus). Ex. 2011, 75:5-10; 79:1-10.

Instead, Grother is directed to a new fast dispersing tablet platform for any drug that is "essentially free or absolutely free of mammalian gelatin." Ex. 1008, Abstract. To this end, Grother describes the issues with using gelatin in formulating fast dispersing dosage forms, such as increased processing times, increased costs, and lack of homogeneity. Ex. 1008, 2-3. Grother describes its invention as eliminating gelatin from the formulations and using modified starches instead, listing the various advantages of modified starches, such as improved stability and strength of the dosage form, allowing the use of sweeteners to improve taste, and elimination of exposure to undesirable agents. Ex. 1008, 3-7; *see also* Ex. 2007, ¶ 87.

Grother is not directed to any particular drug, let alone topically acting

corticosteroids. Six of the eight examples disclosed in Grother do not even include a drug. Ex. 1008, 22-31. Examples 7 and 8 include three drugs, none of which are topically acting corticosteroids. Ex. 1008, 29, 31. Grother also discloses that “[a]ny drug may be used as the active ingredient in the composition of the present invention.” Ex. 1008, 15:19-20. Grother then goes on to list hundreds of drugs in multiple drug classes across six pages. Ex. 1008, 16-21; Ex. 2007, ¶ 88.

Petitioner arbitrarily cites to Grother’s disclosure of corticosteroids, specifically fluticasone and budesonide, but does not acknowledge that Grother does not distinguish between topically acting and systemically acting drugs in the plethora of drugs it lists. Pet., 10; Ex. 1008, 18:15-18; Ex. 2011, 78:4-8. Indeed, fluticasone and budesonide are listed among systemically acting corticosteroids, which are expressly excluded from the scope of the ’729 patent’s claims including hydrocortisone, prednisone, prednisolone, methylprednisolone, dexamethasone and betamethasone. *Compare* Ex. 1001, 3:16-20 *with* Ex 1008, 18:15-19. The other drugs and drug classes disclosed in Grother are also predominantly systemically active drugs. A POSA would therefore understand Grother to disclose a general platform technology, for which any drug may be used, not ODTs containing topical corticosteroids for the treatment of EoE. Ex. 2007, ¶ 89. Thus, Petitioner’s arbitrary selection of budesonide and fluticasone is pure hindsight based on Patent Owner’s claims.

As explained in further detail below, Petitioner does not explain why a POSA would be motivated to look to Grother when looking to formulate treatments for inflammatory conditions of the upper gastrointestinal tract or EoE. Petitioner instead begins with the premise that a POSA would seek to formulate an orally disintegrating solid pharmaceutical composition or orally disintegrating tablet without providing any reasoning as to why a POSA would want to make an orally disintegrating composition for treatment of EoE at all.

3. Singh and Cherukuri

Finally, Petitioner cites to Singh and Cherukuri for disclosing solid orally disintegrating compositions containing budesonide. Pet., 10-11 (citing Exs. 1035, 1036). Petitioner does not rely on either reference as a ground for obviousness. Like Grother, Singh and Cherukuri list numerous classes and types of drugs, and neither Singh nor Cherukuri distinguishes between topical or systemic drugs in their laundry list of drug. Nor does either reference discuss using an ODT to topically deposit a topically active drug on the upper gastrointestinal tract (e.g., esophagus), or how to effectively treat inflammation of the upper gastrointestinal tract. Thus, a POSA would understand Singh and Cherukuri to be directed towards general ODT platforms, and Petitioner's arbitrary selection of budesonide is pure hindsight based on Patent Owner's claims. Ex. 2007, ¶ 90

4. FDA Guidance

Petitioner relies on the FDA Guidance for Grounds 2 and 4 and as general background on ODTs. Pet., 11-12. The FDA Guidance states that ODTs are defined as “[a] solid dosage form containing medicinal substances which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue.” Ex. 1005, 2. The FDA Guidance goes on to state that ODTs disintegrate within “approximately 30 seconds or less, when based on the United States Pharmacopeia (USP) disintegration test method or alternative[.]” Ex. 1005, 2. As explained by Petitioner’s expert, the FDA Guidance simply provides a definition for ODTs and is not directed to formulations for treating inflammation of the upper gastrointestinal tract. Ex. 2011, 56:15-21; *see also* Ex. 2007, ¶ 86. Thus, Petitioner’s reliance on the FDA Guidance is driven by pure hindsight as it has no relevance to the problems solved by the ’729 patent, namely topically depositing a corticosteroid on the upper gastrointestinal tract to treat inflammatory conditions thereof, such as EoE.

B. No Motivation to Begin with an ODT when Solving the Problem of Delivering Topically Acting Corticosteroid to Upper Gastrointestinal Tract

In analyzing the scope of the prior art from the lens of hindsight, Petitioner begins its obviousness analysis with ODTs. A POSA trying to treat inflammation of the upper gastrointestinal tract, however, would have began by first identifying formulations that were effective for treating inflammation of the upper

gastrointestinal tract, which may not necessarily have been an orally disintegrating solid pharmaceutical composition.

First, from the disclosure in Dohil and the “off-label” treatments addressed in the ’729 patent, a POSA would understand that liquid and aerosolized formulations were known to deliver an effective amount of a corticosteroid to the upper gastrointestinal tract. Ex. 1002, [0006], [0046]-[0070]; Ex. 1001, 1:30-41. Further, from Dohil, a POSA would understand that a large volume of viscous liquid can provide pan-esophageal coverage and increase the duration of contact of the topical corticosteroid to the inflamed esophagus. Ex. 1002, [0031], [0053], [0067]. Indeed, as discussed above, each of Dohil’s examples show that the viscous liquid formulations of budesonide are effective to treat EoE.

Thus, a POSA would start with Dohil’s liquid. A POSA would have no motivation to fundamentally change Dohil’s liquid composition and formulate budesonide as a solid composition. Such a modification would change the principle operation of Dohil’s liquid formulation, which is not an obvious modification. MPEP § 2143.01 (IV) (“If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious.”) (citing *In re Ratti*, 270 F.2d 810, 813, 123 USPQ 349, 352 (C.C.P.A. 1959)).

Assuming a POSA would formulate budesonide as a solid composition, it would not be an orally disintegrating composition that disintegrates within 60 seconds as claimed in the '729 patent. Given Dohil's teaching that a large volume of viscous liquid (8-12 mL) and prolonged esophageal contact is necessary for efficacy, a POSA would therefore be motivated to provide longer disintegration times to increase contact with the esophagus, such as with Dohil's lozenge which would dissolve slowly. ODTs that disintegrate within 60 seconds or 30 seconds would therefore be counterintuitive. Thus, Petitioner's analysis begins from a flawed premise.

Petitioner's motivation fares even worse under Grother. Grother is not directed to treating any particular disease, much less inflammation of the gastrointestinal tract. Ex. 2011, 75:5-10, 79:1-10. While Grother lists corticosteroids in its laundry list of actives that could be used with its new fast dispersing solid dosage form, there is no reason for a POSA to select budesonide or fluticasone over the hundreds of other drugs listed. Petitioner remarks that one of the advantages of orally disintegrating solid pharmaceutical compositions is the ability of the active ingredient to be absorbed through the mucosa of the gastrointestinal tract, beginning in the mouth. Pet., 2, 6, 8. A POSA would therefore be more motivated to select a systemically acting drug for this benefit over a topically acting corticosteroid, because topically acting corticosteroids are *not*

absorbed whereas systemically acting drugs are.

As outlined below for each ground, Petitioner fails to explain why a POSA would be motivated to formulate a tablet containing a topically acting corticosteroid that disintegrates within 60 seconds when attempting to make an efficacious dosage form for treating inflammation of the upper gastrointestinal tract or EoE.

VI. THE EPO DECISION DOES NOT CONTROL

Petitioner argues that because the EPO found different claims of a European counterpart to the '729 patent obvious over Dohil, so too should the Board. EPO proceedings, however, follow a different process according to different rules and are not binding on U.S. tribunals. The claims in the EPO proceedings were directed specifically to an orally disintegrating tablet containing budesonide. Ex. 1004, 27. Contrary to Petitioner's assertion, the EPO found that the disintegration time of 60 seconds was a "distinguishing" feature over Dohil. Ex. 1004, ¶ 36.4. A "technical effect," however, could not be derived from the examples in the European patent application. Ex. 1004, ¶¶ 36.5, 36.6. According to the EPO, this was because the example related only to fluticasone while the claims were directed to budesonide. Ex. 1004, ¶ 36.6.

The "technical effect" is an EPO requirement to establish the inventive step. There is no such requirement under U.S. patent law for establishing non-obviousness. In the U.S., non-obviousness can be based on lack of motivation or

reasonable expectation of success. As such, Petitioner's reliance on the EPO decision is irrelevant to the proceeding at hand. U.S. courts and the Board routinely reject the relevance of such decisions. *See, e.g., Medtronic, Inc. v. Daig Corp.*, 789 F.2d 903, 907-08 (Fed. Cir. 1986) (refusing to adopt an obviousness holding of a German tribunal regarding a German counterpart patent because "[t]he patent laws of the United States are the laws governing a determination of obviousness/nonobviousness of a United States patent"); *Smith & Nephew, Inc. v. ConvaTec Techs. Inc.*, IPR2013-00097, Paper 76 at 3 (P.T.A.B. Feb. 24, 2014) (declining to enter into the record a European Patent Office decision regarding a European counterpart to a challenged U.S. patent, explaining that "the [EPO] decision does not involve the U.S. patents at issue in these proceedings, is not based on U.S. law, and is thus of limited relevance to the instant proceedings").

VII. THE CLAIMS OF THE '729 PATENT ARE PATENTABLE

A. A POSA would not have been motivated to formulate the claimed orally disintegrating solid pharmaceutical composition / tablet to topically deposit a corticosteroid on the upper gastrointestinal tract based on the teachings in Dohil

In grounds 1 and 3, Petitioner relies on Dohil and Venkatesh to challenge claims 1-7, 15, 20-21, 27, and 29-36 and 8, and 16-18, respectively. Both of these grounds rely on Dohil with the knowledge of a POSA. But a POSA would not have been motivated to formulate the claimed orally disintegrating solid pharmaceutical

composition / tablet to topically deposit a corticosteroid on the upper gastrointestinal tract to treat EoE based on Dohil. This is because Dohil teaches a viscous liquid, prepared with a specific volume and viscosity, provides pan-esophageal coverage and effectively treats EoE. Venkatesh does not cure these deficiencies because the combination of Dohil, the knowledge of a POSA, and Venkatesh would not result in the claimed invention. This is because Venkatesh's particles are coated with a water-insoluble or pH-responsive polymer for the purpose of taste-masking, and the taste-mask coating would prevent the corticosteroid from being topically deposited on the upper gastrointestinal tract. Ex. 2007, ¶¶ 128-132. Thus, Petitioner's grounds 1 and 3 fails and claims 1-8, 15-18, 20-21, 27, and 29-36 are patentable.

1. Dohil Does Not Suggest or Teach Orally Disintegrating Solid Pharmaceutical Compositions / Tablets as Required By Claims 1-8, 15-18, 20-21, 27, and 29-36

Petitioner argues that Dohil discloses an orally disintegrating solid pharmaceutical composition comprising a topically administrable corticosteroid that disintegrates within 60 seconds. Pet., 23-25. Petitioner points to Dohil's disclosure of lozenges and similar tablets that "dissolve rapidly in the mouth or esophagus[.]" Pet., 23 (citing Ex. 1002, [0032]). Petitioner goes on to argue that "[i]t would have been obvious to formulate Dohil's rapidly dissolving lozenge or tablet to disintegrate within 60 seconds" using the USP <701> Disintegration Test based on the FDA Guidance. Pet., 23. According to Petitioner, "[a] POSA seeking to formulate

budesonide into an orally disintegrating pharmaceutical composition would be highly motivated to follow the FDA Guidance that such a composition should disintegrate within 30 seconds or less when tested using the USP <701> Disintegration Test.” Pet., 24. This argument presumes that a POSA would be motivated to make an orally disintegrating composition based on the disclosure in Dohil, which is not true.

As explained above, Dohil is directed to making a viscous liquid budesonide formulation (referred to in Dohil as OVB) for treating EoE. Dohil explains it solves the issues with existing treatments for EoE by formulating budesonide as a viscous liquid. Ex. 1002, [0008]-[0009] (“A *liquid*, long-acting topical corticosteroid preparation is needed.”) (emphasis added). Dohil’s disclosure, therefore, is directed to formulating viscous liquid budesonide formulation and showing that these formulations are effective for treating EoE. Ex. 2007, ¶¶ 93-94.

To this end, Dohil discloses liquid pharmaceutical compositions containing viscosity-enhancing excipients throughout its disclosure and all three examples administer the viscous liquid formulation and treat EoE. Ex. 1002, [0013], [0030], [0031], [0036]-[0070]. In Examples 1 and 2, the patients are administered the viscous liquid formulation daily, and both patients showed improvement of EoE symptoms and complete resolution or normal appearing esophagus after treatment. Ex. 1002, [0046]-[0047]. In Example 3, patients were given the viscous liquid

formulation and 90% of patients showed improvement after treatment. Ex. 1002, [0048], [0053], [0060]. In discussing the efficacy of the viscous liquid formulation, Dohil states the large volume of liquid, about 8-12 mL, provided pan-esophageal coverage, which Dohil attributes to efficacy. Ex. 1002, [0067]. Dohil does not disclose any examples using a solid dosage form. Thus, Dohil teaches that a viscous liquid budesonide suspension is successful in treating EoE. Ex. 2007, ¶ 95.

Dohil mentions solid compositions in only two paragraphs, as a “dissolving tablet”/“dissolving wafer” and “lozenge or similar tablet.” Ex. 1002, [0013], [0032]. The first disclosure of dissolving tablets or wafers could refer to solid forms that are dissolved in water before oral administration and is not necessarily directed to tablets that dissolve in the mouth, as solid dosage forms that are dissolved in water before oral administration were well known dosage forms at the time. *See* Ex. 1017, 181; Ex. 2007, ¶ 96.

Regarding the second disclosure of a lozenge or similar tablet, a POSA would understand this is not a disclosure of an orally disintegrating composition that disintegrates in 60 seconds for several reasons. First, Dohil does not disclose the disintegration rate of the lozenge or similar tablet. While the initial drug release may occur rapidly after oral administration, lozenges – by definition – dissolve slowly, and therefore a “similar tablet” would also dissolve slowly. Ex. 2013, 413; Ex. 2014, 201. Consequently, the disclosure of a lozenge and similar tablet cannot be a

disclosure of an orally dissolving composition that disintegrates in 60 seconds as claimed. Second, the longer disintegration rate of a lozenge or similar tablet is necessary to achieve the 8-12 mL volume of liquid that Dohil teaches provides pan-esophageal coverage and is necessary for effective treatment of EoE. Lastly, as the Petition acknowledges, ODTs are specifically designed for *easy swallowing*. Pet., 7. However, Dohil explains that “for children or other patients that may have *difficulty with a dissolving lozenge*, the lozenge may be ground or otherwise dissolved in a small volume of water or other pharmaceutically suitable liquid[.]” Ex. 1002, [0032] (emphasis added). Therefore, Dohil’s lozenge or similar tablet does not disintegrate within 60 seconds like an ODT, because such a rate of disintegration allows for easy swallowing. If the lozenge or similar tablet must be ground because patients have difficulty administering it, it is not an ODT. Ex. 2007, ¶¶ 97-99.

Petitioner also argues that a lozenge can be formulated with a disintegrating agent to achieve rapid disintegration. Pet., 21. Petitioner’s own reference, Dankwerts (Ex. 1017), expressly contradicts this argument. Dankwerts teaches that lozenges are manufactured “*without disintegrants* and are intended to be sucked by patients.” Ex. 1017, 181 (emphasis added); *see also* Ex. 2013, 413 (“Disintegrants are not used in the formulation...”). Because lozenges are sucked on and dissolve slowly, Dankwerts states that lozenges are “popular drug delivery system for treating

local mouth diseases and sore throats.” Ex. 1017, 181. Thus, a POSA would understand Dohil to teach a lozenge that dissolves or disintegrates slowly and continuously releases budesonide over time, allowing for continuous treatment as the drug is swallowed over time. Ex. 2007, ¶ 100. As acknowledged by Petitioner’s expert, the mere reference to a disintegrant does not teach or suggest an orally disintegrating composition / tablet because conventional (non-orally disintegrating) tablets include disintegrants. Ex. 2011, 65:2-11.

Accordingly, Petitioner misunderstands and misstates Dohil’s teachings of a lozenge or similar tablet. Thus, Dohil does not teach or suggest a solid orally disintegrating pharmaceutical composition that disintegrates within 60 seconds for at least the reasons stated above.

a. No Motivation to formulate an orally disintegrating solid pharmaceutical composition / tablet based on the teachings of Dohil

As explained above, a POSA would have understood the lozenge mentioned in Dohil to dissolve or disintegrate slowly to allow for continuous topical administration of budesonide to the esophagus for the treatment of EoE. However, Petitioner asserts that “[i]t was desirable for the disintegration time of rapidly dissolving solid compositions to vary ‘from several seconds to about a minute’” and that it would have been obvious to formulate Dohil’s lozenge or similar tablet to

disintegrate within 60 seconds in view of the FDA Guidance. Pet., 23 (citing Ex. 1018, 434).

Petitioner articulates no rationale that would have motivated a POSA to formulate an ODT based on the disclosure in Dohil. As discussed above in Section V.A.1, because Dohil's liquid formulation is effective, palatable, and simple, it is only through impermissible hindsight, guided by the teachings of the '729 patent, that a POSA would have been motivated to combine or modify Dohil to formulate an orally disintegrating pharmaceutical solid composition / tablet that disintegrates within 60 seconds. Ex. 2007, ¶¶ 102-107. "The invention must be viewed not with the blueprint drawn by the inventor, but in the state of the art that existed at the time." *Interconnect Planning Corp.*, 774 F.2d at 1138. An obviousness combination is only legitimate if the petition provides an "explanation as to how or why the references would be combined to arrive at the claimed invention," failing which "we are left with only hindsight bias that *KSR* warns against." *Metalcraft of Mayville, Inc. v. The Toro Co.*, 848 F.3d 1358, 1367 (Fed. Cir. 2017). Petitioner and its expert fail to provide such an explanation, instead jumping to the conclusion that a POSA would seek to formulate a topical corticosteroid into an orally disintegrating pharmaceutical solid composition / tablet that disintegrates within 60 seconds based on the passing references of a lozenge in Dohil. Nothing in Dohil suggests or teaches such a formulation.

Neither Dohil, nor Petitioner's expert, identify an issue with the liquid dosage form administered in Dohil. Indeed, Dohil's viscous liquid has several benefits, namely palatability and efficacy from pan-esophageal coverage. Ex. 2007, ¶ 104. Further, as Petitioner's expert admitted in his deposition testimony, Dohil does not disclose any issues with dosing, compliance or stability with its OVB, and the data disclosed in Dohil shows that OVB is effective in treating EoE. Ex. 2011, 72:25-74:6. Without a recognized problem with the liquid formulation, a POSA would have had no motivation to modify Dohil's viscous liquid dosage form to an orally disintegrating solid pharmaceutical composition / tablet based on the disclosure in Dohil. Ex. 2007, ¶¶ 104-105. More specifically, a POSA would have no motivation to fundamentally change Dohil's efficacious liquid dosage form, by making a significantly more complicated orally disintegrating composition for no apparent reason, particularly when there is no evidence in the prior art that an orally disintegrating composition had been used to topically deposit a topically active drug to the upper gastrointestinal tract. Ex. 2007, ¶¶ 104-105. Petitioner's expert characterizes Dohil's examples as a "proof of concept study" or "pilot studies" and stated that Dohil was using a simple formulation to determine if budesonide worked for EoE. But this statement is illogical and inconsistent with the background literature Petitioner's expert cited to show that budesonide was known to be effective in treating inflammatory conditions, including EoE. Ex. 2011, 61:21-62:3.

Nor does Petitioner or its expert explain why a POSA would be motivated to modify a lozenge or similar tablet to disintegrate within 60 seconds or 30 seconds using the USP <701> Disintegration Test as disclosed in the FDA Guidance. Because lozenges and similar tablets are designed to dissolve slowly (Ex. 2013, 413; Ex. 2014, 201), modifying these dosage forms to disintegrate within 60 seconds based on the FDA Guidance would render the lozenge and similar tablet unsatisfactory for its intended purpose or change the principal operation of dissolving slowly to provide a continuous treatment. Ex. 2007, ¶¶ 105-106; *see* MPEP § 2143.01 (V) (“If a proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, there may be no suggestion or motivation to make the proposed modification”) (citing *In re Gordon*, 733 F.2d 900, 221, USPQ 1125 (Fed. Cir. 1984)); *see also* MPEP § 2143.01 (VI) (“If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious.”) (citing *In re Ratti*, 270 F.2d 810, 813, 123 USPQ 349, 352 (C.C.P.A. 1959)).

Instead of offering any explanation, Petitioner conclusively states that a “POSA seeking to formulate budesonide into an orally disintegrating pharmaceutical composition would be highly motivated to follow the FDA Guidance that such a composition should disintegrate within 30 seconds or less when tested using the USP

<701> Disintegration Test.” Pet., 24. As discussed above, this is conclusory and pure hindsight, as Petitioner does not explain why a POSA would be motivated to formulate a topical corticosteroid into an orally disintegrating composition in the first place. First, Petitioner’s expert admits that nothing in Dohil indicates any issues with dosing, compliance, or stability, and that the data disclosed in Dohil shows that the “simple” liquid formulation is effective in treating EoE. Ex. 2011, 72:25-74:6, 61:3-9, 66:17-20, 68:10-12, 68:22-24, 70:8-12. Thus, a POSA reading Dohil would be motivated to formulate budesonide in a liquid formulation. Assuming that a POSA would formulate budesonide in a solid dosage form based on Dohil (which Patent Owner does not admit, at least for the reasons discussed herein), nothing in Dohil suggests that a faster disintegration rate than provided by a lozenge according to its art-recognized definition would provide the volume and viscosity that render Dohil’s liquid formulation effective. Thus, there would have been no reason to modify a simple formulation with no recognized problems with dosing, compliance, administration, or stability into an orally disintegrating solid pharmaceutical composition. Ex. 2007, ¶¶ 105-107.

Second, Petitioner’s expert testified that an ODT that disintegrates within 60 seconds would only produce about 1-2 mL of liquid. Ex. 2011, 50:17-24. In contrast, Dohil teaches that 8-12 mL of viscous liquid is necessary to provide the pan-esophageal coverage in order to effectively treat EoE. Thus, an ODT that

disintegrates within 60 seconds would not produce the requisite amount of liquid or viscosity necessary to provide pan-esophageal coverage as disclosed in Dohil. A POSA would therefore would not be motivated to modify a lozenge or similar tablet to formulate an orally disintegrating solid pharmaceutical composition or orally disintegrating tablet that disintegrates within 60 seconds or 30 seconds based on Dohil because a POSA would have been motivated to have longer disintegration times to produce 8-12 mL and provide pan-esophageal coverage. *See DePuy Spine, Inc. v. Medtronic Sofamor Danek, Inc.*, 567 F.3d 1314, 1326 (Fed. Cir. 2009) (“An inference of nonobviousness is especially strong where the prior art’s teachings undermine the very reason being proffered as to why a person of ordinary skill would have combined the known elements[,]” i.e., where a prior art reference “teaches away” from the proposed modification) (citation omitted); Ex. 2007, ¶¶ 105-107.

b. A POSA would not have been motivated to formulate an orally disintegrating solid pharmaceutical composition / tablet based on the teaching of Dohil in combination with Venkatesh

Petitioner asserts in ground 3 that claims 8 and 16-18 are unpatentable over Dohil and Venkatesh. As set out above, a POSA would not have been motivated to formulate an orally disintegrating composition containing a topical corticosteroid that disintegrates within 60 seconds based on the disclosure in Dohil in the first place. A POSA also would not have been motivated to combine Venkatesh with the

formulation in Dohil, because Venkatesh's taste-masking prevents the drug from contacting the mouth and esophagus, whereas Dohil is directed to increase contact of corticosteroids with the esophagus to treat EoE. Petitioner continues to rely on impermissible hindsight.

Venkatesh is not directed to topically acting corticosteroids, treatment of inflammation of the upper gastrointestinal tract, or topical delivery of drugs to the upper gastrointestinal tract. Instead, Venkatesh is directed generally to taste-masking of bitter drug particles administered using an ODT, as confirmed by Petitioner's expert. Ex. 2011, 90:13-92:18; 93:12-16; 94:4-25. Taste-masking involves coating with a drug a water-insoluble polymer like ethylcellulose to prevent the drug from contacting the oral cavity. Ex. 1020, [0009], [0018], [0022], [0027]. Venkatesh also discloses cellulose acetate phthalate and hydroxypropyl methylcellulose phthalate as suitable polymers for taste-masking, which are pH-responsive polymers used for enterically coating drugs. Ex. 1020, [0027]; Ex. 2015, 191, 476. Thus, the taste-masking agents used in Venkatesh prevent the bitter drug from topically contacting the oral cavity and consequently the esophagus, which is the exact opposite of the claimed invention. A POSA would therefore not even consider Venkatesh to be relevant to the claims of the '729 patent. Ex. 2007, ¶¶ 129-131. Thus, Venkatesh does not cure the deficiencies in Dohil because Venkatesh is not directed to the treatment of inflammation of the upper gastrointestinal tract,

corticosteroids, or topical delivery of drugs to the upper gastrointestinal tract.

Neither Petitioner nor its expert explain why a POSA would be motivated to look to Venkatesh. Instead, Petitioner merely states that a POSA would have been motivated to manufacture Dohil's lozenges according to Venkatesh. Pet., 54-57. However, there is no motivation to combine Dohil and Venkatesh, because combining Dohil with Venkatesh would undermine Dohil's intended purpose of administering a corticosteroid to the esophagus (a taste-masked corticosteroid would not contact the esophagus). The combination would also undermine Venkatesh's intended purpose of preventing contact of bitter or poor tasting drugs with the mouth (because Venkatesh's taste-masking coating must be removed). "A proposed modification [is] inappropriate for an obviousness inquiry when the modification render[s] the prior art reference inoperable for its intended purpose." *In re Fritch*, 972 F.2d 1260, 1265 n.12 (Fed. Cir. 1992); *see also In re Ratti*, 270 F.2d at 813 (rejecting "suggested combination of references" that "would require ... a change in the basic principles under which the [primary reference] was designed to operate."); *Plas-Pak Indus., Inc. v. Sulzer Mixpac AG*, 600 F. App'x 755, 758-760 (Fed. Cir. 2015) (*nonprecedential*) (affirming the Board's decision in finding certain claims not unpatentable over obviousness as petitioner's contention that a first reference rendered the claims obvious fundamentally altered the operating principle of the prior art). Rather, the proper inquiry is whether a POSA "would have seen a benefit

to” combining the references. *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 424 (2007). Because Petitioner’s arguments regarding the alleged motivation to combine Dohil with Venkatesh are conclusory and do not explain any benefit to combining the references, they must be rejected. *See In re Magnum Oil Tools Int’l, Ltd.*, 829 F.3d 1364, 1380 (Fed. Cir. 2016) (declaring that “a petitioner cannot employ mere conclusory statements”); Ex. 2007, ¶ 136.

c. A POSA would have no expectation of success based on Dohil and the general knowledge of a POSA alone or in combination with Venkatesh

Petitioner conclusively asserts that a POSA would have had a reasonable expectation of success in formulating budesonide into an orally disintegrating pharmaceutical solid composition / tablet that disintegrates within 60 seconds or 30 seconds based on Dohil’s disclosure and the fact that formulating such compositions would have been routine at the time of the ’729 patent. Pet., 24.

First of all, Petitioner mischaracterizes the state of the art, because Petitioner’s expert was not able to identify a single prior art ODT containing a topically acting drug that deposited the drug topically on the upper gastrointestinal tract. Ex. 2011, 17:8-15. What has never been done cannot be routine.

Further, as explained above, Dohil teaches that 8-12 mL of a viscous liquid is needed to provide pan-esophageal coverage and effectively treat EoE. Unlike Dohil’s liquid formulation, which is swallowed as a bolus dose, a POSA would know

that when an orally disintegrating composition is administered, some of the composition dissolves and is swallowed and some remains in the mouth until the remainder disintegrates. A POSA could not predict based on Dohil's disclosure whether the resulting volume or viscosity of the dissolved tablet would provide pan-esophageal coverage and effectively treat EoE. Ex. 1002, [0011], [0013], [0021] ("It has been found that by administering Budesonide in oral form, in a formulation with increased fluid viscosity, that the corticosteroid was delivered to the esophagus in an effective dose to reduce the inflammation of the esophagus."). Ex. 2007, ¶ 108. Even if a POSA desired to formulate a solid composition based on Dohil, Dohil's lozenge or similar tablet dissolves slowly, and, as explained above, would likely produce more volume than an ODT over time. Nothing in Dohil suggests disintegration within 60 seconds would topically administer the corticosteroid to effectively treat EoE. Dohil's lozenge or similar tablet. Ex. 2007, ¶ 108.

Petitioner's assertion for reasonable expectation of success in combination with Venkatesh fares even worse. First, Petitioner's only argument is that Venkatesh discloses successfully manufacturing orally disintegration compositions and so a POSA would have had a reasonable expectation of success in formulating the claimed orally disintegrating pharmaceutical tablets based on Venkatesh. Pet., 54, 55, 57. Petitioner fails to address the fact that Venkatesh is directed to taste-masking of bitter drug particles in ODTs in general. Ex. 1020, [0002], [0009], [0013]-[0015],

[0018]; *see also* Ex. 2011, 90:13-92:18; 93:12-16; 94:4-25. This means that the taste-masked drug particles are coated such that the drug does not contact the oral cavity, which necessarily prevents topical administration of the active ingredient on the upper gastrointestinal tract. Ex. 2007, ¶¶ 136-137. Petitioner fails to address Venkatesh's taste-masking, much less articulate a reasonable expectation to remove this essential feature from Venkatesh's composition and still achieving a pleasant tasting formulation.

Finally, Petitioner only addresses reasonable expectation of success in Ground 1 once for claim limitation 1[iv], in a conclusive manner, which is also referred back to for claim 2. Pet., 24, 26. Petitioner does not address reasonable expectation of success for any other challenged claim in ground 1. For ground 3, Petitioner only makes conclusory statements regarding reasonable expectation of success. Pet., 54, 55, 57. For this reason alone, Petitioner's arguments and evidence are insufficient to render the challenged claims obvious because the reason to combine and reasonable expectation of success must be support by reasoned explanation and evidence, not conclusory statements. *KSR*, 550 U.S. at 418; *In re Magnum*, 829 F.3d at 13780 *Intelligent Bio-Sys., Inc. v. Illumina Cambridge Ltd.*, 821 F.3d 1359, 1367-68 (Fed. Cir. 2016).

d. Dohil Does Not Disclose the Claimed Doses in the Context of a Solid Composition (Claims 1[i], 27[i])

Dohil also does not disclose the specific dose ranges required by claims 1 and 27. Liquid compositions and solid compositions differ in composition and delivery mechanism and therefore require different considerations when determining the proper dose of an active drug. Petitioner cites to Dohil's disclosure of the doses administered to patients in Examples 1-3. Pet., 20. But the patients in Examples 1-3 were given the viscous liquid formulation and Petitioner does not address the difference in formulation or the fact that doses for liquid compositions are not necessarily the same as a solid compositions. Dohil therefore does not disclose any dose for an ODT based on its liquid compositions or teach a POSA how to extrapolate from a liquid to a solid. Ex. 2007, ¶¶ 109-110.

Nor, as discussed above, is there any motivation to formulate an orally disintegrating composition based on Dohil, let alone with the claimed dose range and Petitioner does not address reasonable expectation of success of formulating an orally disintegrating composition with the claimed doses.

a. Dohil Does Not Disclose the Claimed Methods for Treatment (Claims 29-34)

Similarly, Dohil does not disclose the method claims in claims 29-34 of the '729 patent. As discussed above, Dohil does not disclose an orally disintegrating composition that disintegrates within 60 seconds and contains a topical

corticosteroid for the treatment of the upper gastrointestinal tract and therefore cannot disclose methods of treating inflammation of the upper gastrointestinal tract recited in claims 20-34 by administering an orally disintegrating pharmaceutical composition.

There would also be no reasonable expectation of success in treating the inflammation of the upper gastrointestinal tract recited in claims 20-34 by administering an orally disintegrating pharmaceutical composition. As discussed above, Dohil prepared a liquid formulation to have a specific volume and viscosity to achieve pan-esophageal coverage and treat EoE (Ex. 1002, [0067] (“It may have advantages over other therapies in that it is palatable, its volume (8-12 ml) provides pan-esophageal mucosal coverage and it requires only once daily administration.”)). An orally disintegrating composition that disintegrates within 60 seconds would not achieve the volume or viscosity that Dohil teaches provides pan-esophageal coverage and is efficacious. Therefore, there would be no reasonable expectation of success. Ex. 2007, ¶¶ 111-112.

a. Dohil and Venkatesh Do Not Render Obvious Claims 16-18

For the reasons discussed above, Dohil and Venkatesh do not disclose an orally disintegrating pharmaceutical composition or tablet containing a topical corticosteroid that is deposited topically on the upper gastrointestinal tract as

claimed by the '729 patent. Petitioner cites to Venkatesh's disclosure of rapidly dispersing microgranules and drug particle size. Pet., 54-57. As described above, Venkatesh's rapidly dispersing microgranules and drug particle sizes are used for ODTs containing taste-masked drugs for the purposes of improving taste and mouth feel. As discussed above, taste-masking would prevent the corticosteroid from being topically deposited in the upper gastrointestinal tract and would not result in the claimed invention. Thus, there would be no motivation to combine Dohil and Venkatesh to arrive at claims 16-18. Ex. 2007, ¶ 138.

B. A POSA would not have been motivated to formulate an orally disintegrating solid pharmaceutical composition / tablet containing a topical corticosteroid based on the teachings in Grother and the FDA Guidance

In Grounds 2 and 4, Petitioner relies on Grother, the FDA Guidance, and Venkatesh to challenge claims 1-7, 9-15, 20, 27-28, 35-36, and 38-40 and 8, 16-26, and 37 respectively. Both of these grounds rely on Grother and the FDA Guidance, but a POSA would not have been motivated to formulate an orally disintegrating solid pharmaceutical composition / tablet with a topical corticosteroid to topically deposit the corticosteroid on the upper gastrointestinal tract to treat inflammation (e.g., EoE), because neither Grother nor the FDA guidance suggest that an ODT can be used to topically deposit a topical/non-systemic drug on the upper gastrointestinal tract. Ex. 2007, ¶¶ 113-123. Venkatesh does not cure these deficiencies because the

combination of Grother, FDA Guidance and Venkatesh would not result in the claimed invention. This is because Venkatesh's drug particles are coated with a water-insoluble or pH-responsive polymer for the purpose of taste-masking, and this taste-masking coating would prevent the corticosteroid from being topically deposited on the upper gastrointestinal tract. Ex. 2007, ¶¶ 139-149 Thus, Petitioner's ground 2 and 4 fails and claims 1-28 and 35-40 are patentable.

1. Grother and the FDA Guidance are General References and Do Not Teach or Suggest the Orally Disintegrating Solid Pharmaceutical Composition / Tablet as Required By Claims 1-28 and 35-40

Petitioner argues that Grother discloses fast dispersing dosage forms that contain budesonide. Pet., 34-35, 36. Petitioner points to Grother's disclosure that "[a]ny drug may be used as the active ingredient in the composition of the present invention," which includes corticosteroids. Pet., 36 (citing Ex. 1008 15:19-20; 18:15-18). As laid out above, Grother is not directed to any disease, but rather focused on eliminating mammalian gelatin from its disclosed fast dispersing solid dosage forms. Ex. 2011, 75:5-10; 79:1-10; Ex. 1008, Abstract. A POSA would therefore understand that Grother discloses a general ODT platform for which any drug could be used as an active ingredient. EX1008 15:19-20; Ex. 2007, ¶ 115.

While Grother lists corticosteroids among hundreds of drugs, Grother also does not highlight the topical corticosteroids it lists or distinguish between

systemically acting drugs from topically acting drugs with no systemic activity. Ex. 2011, 78:4-18. To the contrary, Grother comingles topically acting corticosteroids with systemically acting corticosteroids that are excluded by the claims. *Compare* Ex. 1001, 3:16-20 *with* Ex 1008, 18:15-18. Notably, Grother does not teach or suggest that its fast dispersing dosage form is capable of topically depositing a topically acting drug on the upper gastrointestinal tract. Ex. 2011, 75:5-10; 79:1-10. Thus, nothing in Grother points to formulating an orally disintegrating solid pharmaceutical composition or orally disintegrating tablet with a topical corticosteroid for the treatment of inflammation of the upper gastrointestinal tract or EoE. A POSA would thus understand that Grother did not recognize, and therefore did not teach or suggest, that orally disintegrating compositions could be used to topically administer a topical corticosteroid to the upper gastrointestinal tract or esophagus for the treatment of EoE. Ex. 2007, ¶¶ 115-118.

The FDA Guidance does not cure this deficiency in Grother. Rather, as explained above and as acknowledged by Petitioner's expert, the FDA Guidance merely provides a definition of ODTs. Ex. 2011, 56:15-21. The FDA Guidance does not address any particular disease, such as EoE, any particular class of drugs, such as corticosteroids, or recognize the use of ODT to topically deposit topically acting drugs on the upper gastrointestinal tract. Ex. 2011, 55:14-23. All the FDA Guidance does, therefore is provide a POSA with the general definition of ODTs.

Ex. 2011, 56:15-21. The generalized disclosures in Grother and the FDA Guidance therefore cannot disclose the required claim limitations of the '729 patent. Ex. 2007, ¶¶ 113-123.

- a. **A POSA had no motivation to formulate an orally disintegrating solid pharmaceutical composition / tablet containing a topical corticosteroid for the treatment of inflammation of the upper gastrointestinal tract based on Grother in view of the FDA Guidance**

Petitioner again uses impermissible hindsight to support its conclusory arguments for motivation to combine. As explained above, a POSA would have understood Grother to disclose a general ODT platform that is not directed to any disease or particular drug. Ex. 2007, ¶ 118. Similarly, a POSA would understand the FDA Guidance to supply a definition for ODTs. Ex. 2007, ¶ 86; Ex. 2011, 56:15-21. Petitioner argues that a POSA “would have been motivated to select budesonide as an active ingredient in Grother’s fast dispersing solid dosage form based on Grother’s express disclosure to do so.” Pet., 36. Petitioner asserts that this would not require a “leap of inventiveness.” Pet., 36 (citing *Boston Sci. Scimed, Inc. v. Cordis Corp.*, 554 F.3d 982, 991 (Fed. Cir. 2009)). But Petitioner misstates the law. “Disparate embodiments in one reference can only be combined if they are a ‘predictable variation’ of each other that does not ‘require a leap of inventiveness.’” *Apple Inc. v. Corephotonics, Ltd.*, Case IPR2018-01348, 2019 WL 3714167, at *2

(P.T.A.B. Aug. 5, 2019) (Paper 11) (quoting *Boston Sci. Scimed, Inc. v. Cordis Corp.*, 554 F.3d 982 (Fed. Cir. 2009)).

Grother cites hundreds of drugs across six pages. Ex. 1008, 16-21. While corticosteroids are listed, Grother does not highlight them in any way or distinguish between systemic and topical corticosteroids. Ex. 1008, 18:15-18. Rather, systemic and topical corticosteroids are contained in the same list, with no distinction. *Id.* The most that can be said about the corticosteroids listed in Grother is that it is included in a long list of other classes of drugs. Ex. 1008, 16-21. The drugs in Grother span a vast variety of drug classes, from analgesics to vaccines and stimulants, the overwhelming majority of which are systemically active and are absorbed through the lower gastrointestinal tract. *Id.* Petitioner does not and cannot argue that the various drugs listed in Grother are “predictable variations” of each other. Because of the wide array of drugs disclosed, and the lack of guidance on formulating an orally disintegrating composition with a topically acting drug for topical deposition on the upper gastrointestinal tract, the Petitioner’s arbitrary selection of budesonide and fluticasone cannot be a “predictable variation,” and Patent Owner’s claims involve a leap of inventiveness. Ex. 2007, ¶¶ 117-120.

It is clear that Petitioner has arbitrarily picked budesonide and fluticasone from Grother’s non-limiting list simply because these drugs are recited in the claims of the ’729 patent. Ex. 2007, ¶¶ 119. The “rationale ... that a person of ordinary

skill would ‘pick and choose’ features from various embodiments of [a single reference], simply because they are in the same [reference], is insufficient to demonstrate a reasonable likelihood of prevailing on this challenge[.]” *LG Display Co. v. Innovative Display Techs. LLC*, Case IPR2014-01362, Paper 12, at 13 (P.T.A.B. Mar. 2, 2015).

Petitioner’s reliance on the FDA Guidance does not provide the requisite motivation that is absent from *Grother*. Instead of offering any explanation, Petitioner recites that a “POSA seeking to formulate budesonide into an orally disintegrating pharmaceutical composition would be highly motivated to follow the FDA Guidance that such a composition should disintegrate within 30 seconds or less when tested using the USP <701> Disintegration Test.” Pet., 40. As discussed above, Petitioner does not explain why a POSA would be motivated to formulate a fast dispersing dosage form containing budesonide for topical deposition on the upper gastrointestinal tract based on *Grother* in the first place, and the FDA Guidance is silent regarding topical corticosteroids or topical deposition of any active on the upper gastrointestinal tract. The Petitioner’s conclusory statements must be rejected. “To satisfy its burden of proving obviousness, a petitioner cannot employ mere conclusory statements. The petitioner must instead articulate specific reasoning, based on evidence of record, to support the legal conclusion of obviousness.” *In re Magnum*, 829 F.3d at 1380.

Thus, because Grother discloses a plethora of drugs to be used in its fast dispersing solid dosage form, and the FDA Guidance is silent regarding topical corticosteroids and topical treatment of the upper gastrointestinal tract, a POSA would not have been motivated to choose budesonide or fluticasone as asserted by Petitioner's argument. Petitioner offers no evidence to suggest there is a motivation to use budesonide or fluticasone based on Grother. For this reason, grounds 2 and 4 must fail.

b. A POSA had no motivation to formulate an orally disintegrating solid pharmaceutical composition / tablet containing a topical corticosteroid for the treatment of inflammation of the upper gastrointestinal tract based on Grother in view of the FDA Guidance and Venkatesh

Petitioner asserts in ground 4 that claims 8, 16-26, and 37 are unpatentable over Grother, the FDA Guidance, and Venkatesh. As set out above, a POSA had no motivation to formulate an orally disintegrating solid pharmaceutical composition or orally disintegrating tablet containing a topical corticosteroid that is topically deposited on the upper gastrointestinal tract based on the disclosure in Grother and the FDA Guidance. Venkatesh does not cure these deficiencies, because a POSA also would not have been motivated to combine the teachings in Venkatesh with the formulation in Grother and the FDA Guidance to arrive at the claimed invention. Petitioner continues to rely on impermissible hindsight. Ex. 2007, ¶¶ 144-148.

As explained above, Venkatesh is not directed to a particular disease, the delivery of corticosteroids, or topical delivery of drugs. Venkatesh, like Grother, teaches that its process can be used for “any therapeutic active agent[.]” Ex. 1020, [0025]. No corticosteroids are listed in Venkatesh. Ex. 2011, 87:5-9. Venkatesh, like Grother, does not distinguish between systemic and topical drugs or recognize that an ODT can be used to topically deposit a topically acting drug to the upper gastrointestinal tract. Ex. 2011, 88:7-11. Based on this alone, a POSA would not consider Venkatesh to be relevant to the claims of the '729 patent and would not be motivated to combine Venkatesh with Grother and the FDA Guidance, and arrive at the claimed invention.

Not only does Venkatesh not disclose topical corticosteroids, Venkatesh's ODT cannot be used to topically deposit a topically acting drug to the upper gastrointestinal tract. Venkatesh is directed generally to taste-masking of bitter drug particles in ODTs, as confirmed by Petitioner's expert. Ex. 2011, 90:13-92:18; 93:12-16; 94:4-25. Venkatesh's taste-masking prevents the bitter drug from contacting the oral cavity, and consequently would prevent the topically acting corticosteroid from topically contacting the inflamed esophageal tissue, as required by the claims of the 729 patent. Ex. 2007, ¶¶ 144-148. Because the combination of Venkatesh, Grother, and FDA Guidance does not result in the claimed invention, there is no motivation to combine Venkatesh, Grother, and FDA Guidance.

Petitioner fails to address Venkatesh's taste-masking, much less articulate a motivation to remove this essential feature from Venkatesh's ODT. Nor could Petitioner provide this motivation, because removing Venkatesh's taste-masking layer would render Venkatesh's ODT unsatisfactory for its intended purpose of providing a taste-masked ODT. MPEP § 2143.01 (V) ("If a proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, there may be no suggestion or motivation to make the proposed modification.") (citing *In re Gordon*, 733 F.2d 900, 221, USPQ 1125 (Fed. Cir. 1984)).

Neither Petitioner nor its expert explain why a POSA would be motivated to look to Venkatesh. Instead, Petitioner merely states that a POSA would have been motivated to manufacture Grother's fast dispersing solid dosage form according to Venkatesh. Pet., 60-68. Because Petitioner's arguments regarding the alleged motivation to combine Grother and the FDA Guidance with Venkatesh are conclusory and do not explain any benefit to combining the references, they must be rejected. *See In re Magnum*, 829 F.3d at 1380 (declaring that "a petitioner cannot employ mere conclusory statements"). A POSA had no expectation of success based on Grother and the FDA Guidance alone or in combination with Venkatesh.

Petitioner does not even attempt to explain why a POSA would have a reasonable expectation of success in formulating an orally disintegrating

pharmaceutical composition containing budesonide or fluticasone that would topically deposit budesonide or fluticasone on the upper gastrointestinal tract based on Grother's disclosure and the FDA Guidance. The most Petitioner can offer is that formulating orally disintegrating pharmaceutical compositions were routine at the time of the '729 patent. Pet., 40, 51. But Petitioner's expert was not able to identify a single prior art ODT containing a topically acting drug that was deposited topically to the upper gastrointestinal track. Ex. 2011, 17:8-15. Grother fails to recognize that an ODT can topically deposit a topically acting drug, such as a corticosteroid, to the upper gastrointestinal tract. As Petitioner's expert acknowledges, the FDA Guidance only provides a definition for ODTs, and thus does not remedy the deficiencies in Grother. Ex. 2011, 56:15-21. Therefore, Petitioner failed to provide any actual evidence that a POSA would arrive at the claimed invention with a reasonable expectation of success.

A POSA would understand that formulations for administering systemic drugs, which are absorbed by the lower gastrointestinal tract, differ from formulations that topically administer the drug to a localized area to the upper gastrointestinal tract. Ex. 2007, ¶ 121. A POSA would therefore not reasonably expect to successfully formulate an orally disintegrating pharmaceutical composition containing a corticosteroid to topically deposit the corticosteroid on the

upper gastrointestinal tract for treating inflammation of the upper gastrointestinal tract from Grother's disclosure and the FDA Guidance.

Venkatesh does not cure the deficiencies in Grother and the FDA Guidance. Petitioner relies on conclusory assertions that a POSA would have a reasonable expectation of success based on the process disclosed in Venkatesh. Again, Petitioner does not attempt to explain how a POSA would have a reasonable expectation of success in arriving at the claimed invention based on Venkatesh's process, which coats the drug with a water-insoluble or pH-responsive taste-masking layer so that the drug does not contact the mouth or the upper gastrointestinal tract, or why a POSA would have a reasonable expectation of success in removing this essential feature from Venkatesh's composition and still achieve a pleasant tasting formulation.

Because Venkatesh's taste-masking layer would prevent a corticosteroid from contacting the upper gastrointestinal tract, there is no reasonable expectation of formulating an orally disintegrating composition to topically deposit a topically acting corticosteroid on the upper gastrointestinal tract to treat EoE based on Venkatesh, Grother, and FDA Guidance. Ex. 2007, ¶ 148.

c. Grother and the FDA Guidance Do Not Render Obvious the Claimed Doses (Claims 1[i], 27[i], 28, 38-40)

Grother does not disclose the specific dose ranges required by claims 1, 27,

28, and 38-40. Petitioner cites to Grother's disclosure of general dosing, and that the "upper value" is generally 60 mg. Pet., 36. The dosages disclosed in Grother relate to dosing generally, not topically active corticosteroids specifically, and certainly not for a corticosteroid that is topically deposited on the upper gastrointestinal tract to treat inflammation or EoE. Petitioner also cites to various unasserted references disclosing doses for budesonide. Pet., 37 (citing Exs. 1026, 1009, 1002). None of the references disclose an ODT containing budesonide, and nearly all references involve enterically coated compositions that deliver budesonide to the lower gastrointestinal tract. A POSA would understand that formulating an orally disintegrating composition to topically deposit a corticosteroid in the upper gastrointestinal tract would involve different considerations and likely different doses than liquid formulations, enterically coated tablets, and rectal foam. Petitioner fails to explain how Grother discloses the claimed doses for an orally disintegrating solid pharmaceutical composition or orally disintegrating tablet containing a topical corticosteroid based on its general disclosures. Ex. 2007, ¶¶ 122-123.

As discussed above, a POSA would not have any motivation or reasonable expectation of success to formulate an orally disintegrating composition containing a topical corticosteroid with the claimed doses based on Grother and the FDA guidance (which does not disclose any dose for any drug). Dr. Parr conclusively states that a POSA would have a reasonable expectation of success, but does not

explain why or how. Pet., 37, 51. For at least this reason, Petitioner's arguments must be rejected. *See In re Magnum*, 829 F.3d at 1380 (declaring that "a petitioner cannot employ mere conclusory statements").

d. Grother, the FDA Guidance and Venkatesh Do Not Render Obvious Claims 16-19

Petitioner cites to Venkatesh's disclosure of rapidly dispersing microgranules and drug particle size and argues it renders obvious claims 16-19. Pet., 59-63. As described above, Venkatesh's rapidly dispersing microgranules and drug particle sizes are used for ODTs containing taste-masked drugs for the purposes of improving taste and mouth feel. Taste-masking would prevent the corticosteroid from being topically deposited in the upper gastrointestinal tract. As such, the combination of Grother, the FDA Guidance, and Venkatesh would not result in the claimed invention. There would be no motivation to combine Grother, FDA Guidance and Venkatesh to arrive at claims 16-19, or a reasonable expectation of success, for the reasons described above. Ex. 2007, ¶ 149.

VIII. CONCLUSION

For the foregoing reasons, Petitioner has failed to establish that the challenged claims of the '729 patent are unpatentable. Patent Owner respectfully requests the Board find the challenged claims patentable over the grounds in the Petition.

Date: April 21, 2025

Respectfully submitted,

Cooley LLP
ATTN: Patent Group
1299 Pennsylvania Ave., NW
Suite 700
Washington D. C. 20004
Tel: (202) 776-2982
Fax: (202) 842-7887

BY: /Sanya Sukduang/
Sanya Sukduang
Reg. No. 46,390
Counsel for Patent Owner

CERTIFICATE OF COMPLIANCE WITH WORD COUNT

Pursuant to 37 C. F. R. § 42. 24(d), I certify that this response complies with the type-volume limits of 37 C. F. R. § 42. 24(c)(1) because it contains 11,759 words, according to the word-processing system used to prepare this petition, excluding the parts of this response that are exempted by 37 C.F.R. § 42.24(c) (including the table of contents, a table of authorities, an exhibits list, a listing of facts, a certificate of service or this certificate of word count, or appendix of exhibits).

Date: April 21, 2025

Respectfully submitted,

Cooley LLP
ATTN: Patent Group
1299 Pennsylvania Ave., NW
Suite 700
Washington D. C. 20004
Tel: (202) 776-2982
Fax: (202) 842-7887

BY: /Sanya Sukduang/
Sanya Sukduang
Reg. No. 46,390
Counsel for Patent Owner

**CERTIFICATION OF SERVICE
UNDER 37 C. F. R. §§ 42. 6(e), 42. 105(a)**

I, Sanya Sukduang, hereby certify that on April 21, 2025, the foregoing Patent Owner's Response and Exhibits 2007–2015 pursuant to 37 C. F. R. § 42.8 were served electronically via email on the following counsel of record for Petitioner as follows:

Nathanael Luman
Eric S. Furman
Philip J. Minnick
KNOBBE, MARTENS, OLSON, & BEAR, LLP
2nrl@knobbe. com
2esf@knobbe. com
2pjm@knobbe. com
BoxDRFPGL.001LP@knobbe. com

DATED: April 21, 2025

/Sanya Sukduang/
Sanya Sukduang
Reg. No. 46,390